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Original Contribution

EFFECT OF GALANTAMINE ON THE SHORT MEMORY OF SPONTANEOUSLY HYPERTENSIVE RATS (SHR) EXPOSED TO INSOMNIA

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ABSTRACT

Galantamine has beneficial effect on elderly patients with vascular and AD dementia. The influence of this drug on the major disease of patients with hypertension and insomnia, is still not estimated.
The effect of galantamine on the short-time memory of normotensive and spontaneously hypertensive rats in model of insomnia, was investigated. Data suggested that insomnia might contribute to further development of hypertension and memory decline in patients with dementia. Galantamine might help to improve the cognitive capabilities, but its effect on the blood pressure and heart rate is not significantly beneficial.

Key words: Galantamine, hypertension, insomnia, dementia, cognition.

INTRODUCTION

Insomnia [1] and hypertension [2] are among the most common complications accompanying dementia [3] Due to the higher risk of developing vascular dementia among elderly people with high blood pressure and insomnia, the combination of hypertension, insomnia and dementia is an object of serious discussion and detailed research [4]. Oxidative stress is being detected along with hypertension [5], sleeplessness [6] and correlates with the progress of dementia [7]. Therefore, a therapy of elderly people with medications having antioxidant properties might be highly beneficial. Galantamine slows down the development of the brain degeneration [8] and does not cause insomnia [9] of patients with light to mild AD or vascular dementia. It improves the cognition of normotensive Wistar rats in a model of prolonged alcohol intake [10] and enhanced the antioxidant status of the rat's brain in model of sleep deprivation [11]. The effect of Galantamine on the cognitive abilities of animals with spontaneous arterial hypertension (SHR) being exposed to a sleep deprivation remains unexplored.

In the present work, the effect of Galantamine on the cognition, blood pressure and heart rate of SHR exposed to a sleep deprivation was estimated.

MATERIALS AND METHODS

Twelve male SHR (body weight of 230±40 g, blood pressure of 178±8 mm Hg, heart rate of 382±16 imp/min) were separated in 6 cages. The sleep deprivation of the entire population (with group label "Insomnia") was achieved by exposing them to a constant light. After developing insomnia for one week, their short-time memory was monitored for the next 7 days. Then the large group "Insomnia" vas divided into two smaller groups, 6 animals each. During the following week, a group named "Galantamine" received galantamine (i.p., SDD 2.5 mg/kg in saline solution), while the "Control" group being treated with saline solution only. The 8-arm Radial Maze task performance of both groups was monitored in a daily basis to the end of the experiment.
Both groups received 10 g per 100 g body weight standard food, and water *ab libitum*.

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The amounts of food and water used, and body weight, were monitored every day. The blood pressure and heart rate were detected every 3-th day, using the tail-cuff method. The short-time memory of the rats was estimated using a 8-arm Radial Maze with 8 baited arms (chocolate baits). Animals were kept in the Radial Maze for 5 minutes. A visit in a baited arm with eating the bait was considered as a right decision. A visit in an unbaited arm was registered as wrong decision related with error of the working memory. The Effectiveness of the performance was calculated by dividing the number of the right decisions to the total number of entries. The Working Memory Errors were estimated by dividing the number of the wrong desi8sions top the total number of entries. The mobility of SHR was characterized by the Average Running Time (the average time in seconds, needed to an animal for making one decision).

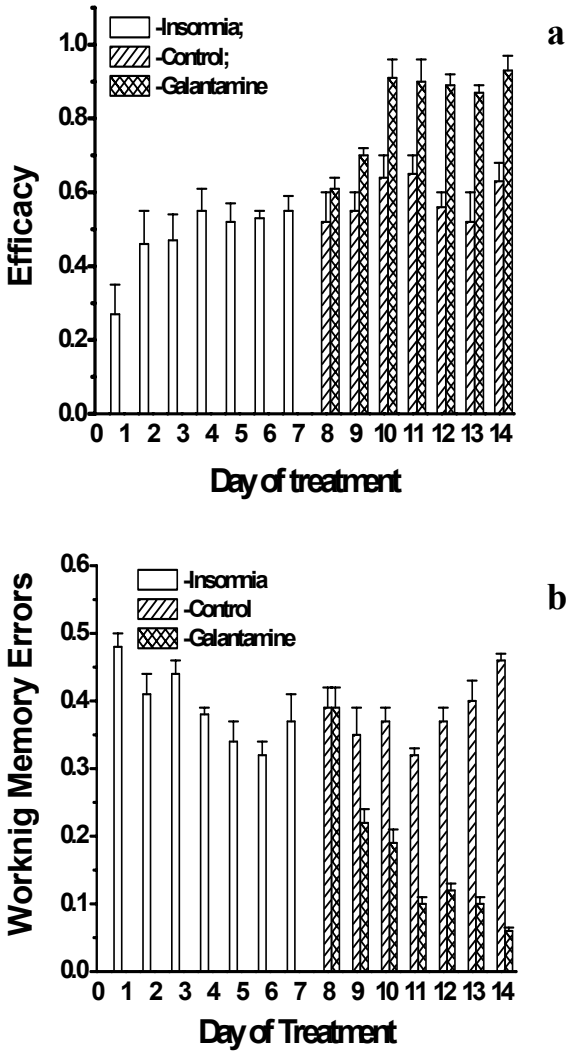

Figure 1: Efficacy (a) and Working Memory Errors (b) of SHR exposed to a sleep deprivation (Insomnia), and these with insomnia being treated with saline solution (Control) or Galantamine (Galantamine).

All animals were treated according the Treatment Protocol accepted in the Medical University of Sofia.

Standard saline solution and Galantamine hydrobromide (Nivalin) 10mg/1ml vials (Production of Sofarma) were used in the experiment.

Statistical analysis was performed using an INSTAT program package, version 2.04. The differences between two groups were estimated by a two-tailed non-parametric t-test with Weltch correction.

RESULTS AND DISCUSSION

The sleep deprivation of SHR for 7 days (group "Insomnia") made the rats very aggressive to each other, and caused an increasing of both blood pressures (from 178±8 to 189±11 mm Hg, p=0.01) and heart rates (from 382±16 to 461±12, p<0.0001). Further administration with saline solution (group "Control") or galantamine (group "Galantamine") did not affect the blood pressures (all comparisons gave p>0.1), but heart rates of group "Control" (420±7 imp/min) were significantly (p=0.003) higher than those of group "Galantamine" (399±6 imp/min), latter still higher (p=0.0054) than those of the animals livind at normal day/night regime (382±16). It was proposed that galantamine may decrease in some extent the heart rate of SHR exposed to insomnia, but is unable to restore completely the value observed in SHR living at normal day/night regime.

The 8 arm Radial Maze task performance of SHR being exposed to a constant light improved to the sixth day and then became worst, mostly because of the increasing of the Working Memory Errors (**Figure 1**). The administration with Galantamine resulted in an increasing of the Effectiveness (**Figure 1-a**) and substantial decreasing of the Working Memory Errors (**Figure.1-b**). The Average Running Time of the group receiving galantamine in the end of the experiment was 6±1 s/run, while this of the Control group was 12±2 sec/run.

Our experiments showed that administration with galantamine of SHR with insomnia improved their short-time memory, increased the efficacy of their action, and their mobility. Its beneficial effect on the heart rate was modest, while no effect on the blood pressure was registered. It might be proposed that Galantamine might delay the memory decline when used by patients with combination of dementia, hypertension and insomnia. It might have a slight positive effect on the heart rate, but no beneficial effect on the hypertension might be expected.

CONCLUSIONS

Sleep deprivation of SHR caused substantial increasing of the blood pressure and heart rate of the animals.

Administration with galantamine of SHR being exposed to insomnia significantly improved their short-time memory.

Galantamine did not show any effect on the high blood pressure, and exhibited slightly decreased the heart rate of SHR being exposed to insomnia.

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